

TOYA151.001APC

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	: Tada, et al.
App. No	: 10/580,882
Filed	: May 26, 2006
For	: EXTERNAL PREPARATION FOR SKIN
Examiner	: Kendra Carter
Art Unit	: 1627
Conf No.	: 7132

DECLARATION UNDER 37 C.F.R. § 1.132

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

I, Akihiro Tada, declare as follows

1. I am an inventor in the above-identified application. I am familiar with the above-referenced U.S. patent application including the Office Action mailed December 9, 2009 and cited reference, Ishida (EP 1 147 764).
2. The inhibitory action of Compound III of Ishida on dendrites of melanocytes was compared with a compound according to the present application. The compound used for comparison was centaureidin (5,7-dihydroxy-3,6-dimethoxy-2-(5-hydroxy-4-methoxyphenyl)-4H-1-benzopyran-4-one of amended claim 1), also known as "Compound 1" in the specification of U.S. Application No. 10/580,882 (present specification).
3. Normal human melanocytes were prepared as described in Test Example 1 of the present specification. Compound III of Ishida and centaureidin were dissolved in dimethylsulfoxide and tested as described in Test Example 1 of the present specification. Results are shown on the attached sheet.

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4. The data shows that the compound of Ishida (Nobiletin) does not have any effect on dendrite length at concentrations from $10^{-4}\%$ to $10^{-6}\%$. In contrast, $10^{-5}\%$ centaureidin strongly inhibits dendrite length. Compounds 2-4 show the same effect as demonstrated in the present specification at Test Example 3, pages 27-28 of the present specification. I conclude that the compounds of Ishida, et al. have a very different effect from the compounds of the claimed invention. The compounds of Ishida, et al. cannot be used to inhibit dendrite length. This different effect is unexpected in view of the structural similarity of these compounds.

5. The claimed compositions also have the advantage that the presence of Compound 1 inhibits cell death when combined with 4-n-butyl resorcinol within the claimed concentration ranges. This effect is shown in Table 5 of the present specification at page 29. It can be seen that the number of live cells decreases as the concentration of 4-n-butyl resorcinol increases in the absence of centaureidin (rows 2, 3, and 4 of Table 5, compare the last column). This effect is reversed by the addition of centaureidin. The effect is dependent upon the concentration of centaureidin as shown by comparing results at 0.1 mM centaureidin (row 8) with 0.5 mM centaureidin ((last) row 12) when concentration of 4-n-butyl resorcinol is maximal (0.5%). By combining centaureidin with 4-n-butyl resorcinol, the whiteness of cells and number of live cells is maximized. This result was unexpected.

6. I declare that all statements made herein of my own knowledge are true and that all statements made on information and belief are believed to be true; and further that these statements were made with the knowledge that willful, false statements and the like so made are punishable by fine or imprisonment, or both, under Section 1001 of Title 18 of the United States codes and that such willful, false statements may jeopardize the validity of the application or patent issuing therefrom.

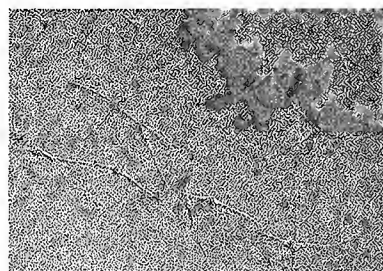
Dated: 02/16/2010

By: Akihiro Tada
Akihiro Tada

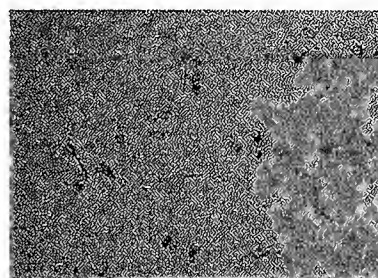
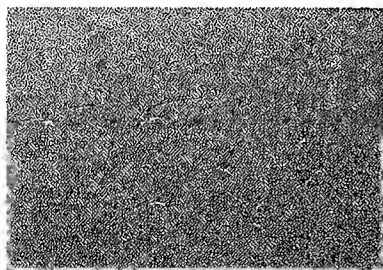
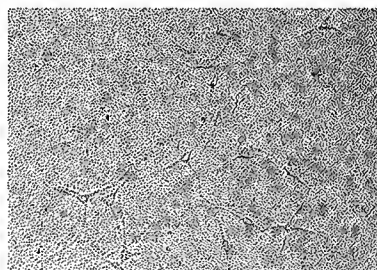
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<Results>

Test compounds		Length of dendrites (μm)
Centaureidin	10^{-5} %	30 ± 10
Nobiletin	10^{-4} %	139 ± 23
Nobiletin	10^{-5} %	142 ± 18
Nobiletin	10^{-6} %	141 ± 30
Control		143 ± 35



Control

Centaureidin 10^{-5} %Nobiletin 10^{-4} %Nobiletin 10^{-5} %Nobiletin 10^{-6} %